

# METHODS AND APPARATUS FOR MASS SPECTROMETRIC ANALYSIS OF CONSTITUENTS IN LIQUIDS

This is a continuing application of application Ser. No. 835,160, filed Sept. 21, 1977, now abandoned.

## BACKGROUND OF THE INVENTION

The invention relates to a method and apparatus for spectrometric analysis of liquids such as may be received from a liquid chromatograph.

In the mass spectral analysis of molecular constituents dissolved or suspended in liquids, a frequently used technique is to place a sample of the liquid on a surface and allow the liquid to evaporate, leaving a solid residue of the molecular components from the liquid. Thereafter this residue is heated to drive the molecules into the vapor phase, after which the molecules are ionized by electron impact. The ions are then analyzed for their mass-to-charge ratio using ion separation in magnetic fields, time varying quadrupole electrical fields or other ion mass spectrometer techniques.

This approach is satisfactory if the molecule is sufficiently volatile to enter the vapor phase prior to undergoing thermal decomposition.

For those molecules which thermally decompose before evaporating, another technique is to place a drop of liquid on an array of very fine needle points or sharp edges of an electrically conducting material and then apply a high voltage to the material. The very strong electric fields in the immediate vicinity of the points or edges assist the molecules in leaving the surface and furthermore when a molecule leaves it is as an ion, i.e. an electrically charged molecule. These techniques, which are often used in conjunction with heating, are called Field Ionization and Field Desorption Ionization.

The present invention utilizes another method to produce gaseous ions, of both volatile and nonvolatile molecular constituents of liquids, which incorporates a technique called "electrospray." Although it applies generally to liquids which can evaporate, it is of particular interest when used to couple mass spectrometers to liquid chromatographs.

Gas chromatographs and liquid chromatographs are used to separate mixtures of molecules which are then detected in an appropriate manner. A commonly used instrument at present is the gas chromatograph-mass spectrometer (GC/MS) combination where the detector is a mass spectrometer.

Gas chromatographs require that the molecules be volatile so that they can be suspended in the carrier gas used in the gas chromatograph and high temperatures of up to several hundred degrees Celsius are required in some cases to volatilize the molecules in the sample detected. Although this is satisfactory for many molecules, many other molecules of interest to the analytical chemist or biologist tend to decompose at high temperatures before they are volatilized.

The liquid chromatograph is similar to a gas chromatograph except that a liquid is used as the carrier substance rather than a gas. In the liquid chromatograph the sample molecules are suspended in a liquid at low temperature, so that there is no tendency for the molecule to decompose thermally. The problem with coupling a liquid chromatograph, which separates the molecules in a mixture, with a mass spectrometer which uniquely identifies each of the molecule components in

the mixture is first of getting the molecules into the vapor phase and next electrically charging the molecules, either positively or negatively, to form ions which can then be separated in the charge-to-mass analyzer of the mass spectrometer.

A method of accomplishing the task of simultaneous volatilizing and charging molecules which makes use of electrospray techniques is described by Malcolm Dole and his associates (Journal of Chemical Physics, Volume 49, page 2240 (1968) and Volume 52, page 4977 (1970)). In the technique, a liquid is passed through a capillary tube made of metal on which a high voltage is placed. As the liquid emerges from the capillary, it is subjected to a very strong electric field in the vicinity of the end of the capillary. The strong field polarizes the liquid at the end of the capillary, causing an elongated liquid filament to be formed and then normal surface tension forces produce instabilities which snap off a length of the filament to form a small droplet. Inasmuch as the snapping off of the filament occurs while the filament is in the strong electric field, the droplet formed is highly charged electrically. The electric fields acting on the charged droplet tend to accelerate the droplet away from the end of the capillary.

If the liquid is volatile it tends to evaporate and the droplet diminishes in size. If no charge leaks off the droplet while it is evaporating, the charge density on the surface of the droplet increases. When the surface charge density is low, the surface tension forces which tend to hold the droplet together in a spherical shape exceed the electrical repulsive forces caused by the surface charge density, and the droplet retains a spherical shape. However, as the droplet evaporates without loss of charge, there is a point reached where the electrical repulsive forces exceed the attractive surface tension forces whereupon the droplet becomes unstable and tends to break up into two or more smaller charged droplets. This point is called the Rayleigh instability limit and is characterized by the formula

$$n = (2\pi TD^3)^{1/2} / e$$

where  $n$  is the total number of electronic charges on the droplet,  $e$  is the electronic unit of charge ( $1.6 \times 10^{-19}$  coulombs),  $T$  is the surface tension and  $D$  is the diameter of the droplet. (Lord Rayleigh, Philosophical Magazine, Vol. 14, page 184 (1882)).

It has occurred to the inventor that these effects may be advantageously utilized for the purpose of producing gaseous ions of constituents of liquids including ions of molecules suspended or dissolved in a carrier liquid of liquid chromatographs. The molecular ions so produced then may be analyzed on the basis of their mass-to-charge ratio.

## SUMMARY OF THE INVENTION

In the instant invention, a carrier liquid containing molecules to be analyzed, which includes molecules of a sample to be analyzed in the case of the liquid being the carrier liquid of a liquid chromatograph, is caused to flow under external pressure through a capillary tube of small bore. The capillary tube is composed of metal or other conducting material and is placed at a high electric potential ranging from a few hundred volts to several ten thousands of volts. The end of the capillary tube protrudes into a small chamber, the interior of which is placed at a low potential in the range of a few volts to several hundred volts. The strong electric field between